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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Chiaki Senoo et al.	Confirmation No.:	1189
Serial No.:	09/831,180	Art Unit:	1652
371(c) Date:	August 3, 2001	Examiner:	S. Swope
Customer No.:	21559		
Title:	NOVEL TRYPSIN FAMILY SERINE PROTEASES		

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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Applicants respectfully request review of the final rejection set forth in the final Office action mailed on February 13, 2007 in connection with the above-captioned patent application. No amendments are being filed with this request, and this request is being filed with a Notice of Appeal.

The review is requested for the reasons set forth below.

REMARKS

Claims 1-2 and 4-8 stand rejected under 35 U.S.C. § 101 and § 112, first paragraph, for lack of patentable utility. Applicants submit that the presently-claimed invention possesses specific, substantial, credible, and well-established utility, as described below; accordingly, the utility rejection should be withdrawn and the case allowed.

In the Office action mailed on May 23, 2006, the Office states (page 4):

> The specification fails to teach a specific and substantial function for the protein set forth by SEQ ID NO: 2, as encoded by SEQ ID NO: 1. Based on the specification, page 1, paragraph 1, the asserted utility for said protein is as a trypsin-family serine protease. Said assertion for the protein of SEQ ID NO: 2 is not supported by any experimental evidence; for example, analysis of the protein for protease activity....

Applicants disagree with this basis of rejection. As an initial matter, the Utility Examination Guidelines (66 F.R. 1092, 1092-1099) and Revised Interim Utility Guidelines Training Materials (hereinafter "the Training Materials") outline the criteria to determine the utility of an invention. Utility must be specific, substantial, and credible; furthermore, utility may either be disclosed in the specification or may be recognized as well-established in the art.

In the reply filed on November 24, 2006 (pages 11-12), applicants direct the Office's attention to Example 10 of the Training Materials. This Example asks whether there was a "well established utility" for the claimed invention: a nucleic acid including a particular sequence homologous to a DNA ligase. The Training Materials answer this question as follows (pages 54-55, emphasis added):

> Based upon applicant's disclosure and the results of the PTO search, there is no reason to doubt the assertion that SEQ ID NO: 2 encodes a DNA ligase. ***Further, DNA ligases have a well-established use in the molecular biology art based on this class of protein's ability to ligate DNA.*** Consequently the answer to the question is yes...In this case SEQ ID NO: 2 was shown to encode a DNA ligase that the artisan would have recognized as having a specific, substantial and credible utility based on its enzymatic activity.
>
> Thus, the conclusion reached from this analysis is that a 35 U.S.C. § 101 rejection and a 35 U.S.C. § 112, first paragraph, utility rejection should not be made.

The present invention and supporting specification are highly analogous to the above-described Example 10 of the Training Materials. In the present case, the class of protein to

which the claimed proteins belong is trypsin-family serine proteases, rather than DNA ligases, and the methodology used to identify SEQ ID NO: 2 as a member of this class uses signature motifs rather than relying solely on sequence alignment. Nevertheless, the same fundamental reasoning should apply: just as in the Training Guidelines Example, here applicants have identified a specific, substantial, and credible utility for the presently-claimed invention by identifying it as a member of a class of enzymes that possesses a specific activity. Thus, a rejection for lack of patentable utility should not be made.

In the Supplemental Reply filed on January 10, 2007 (pages 2-3), applicants direct the Office's attention to page 36, lines 25-33, of the specification as filed, which states:

> Based on the analytical search of the GCG, the amino acid sequence was proved to contain two types of trypsin-family serine protease motifs, "Trypsin-His (PROSITE PS00134)" and "Trypsin-Ser (PROSITE PS00135)". PROSITE indicates "if a protein includes both the serine and histidine active site signatures, the probability of it being a trypsin family serine protease is 100%" [citation omitted]. "Tespec PRO-1" therefore can be regarded as a trypsin-family serine protease.

Applicants conclude (page 4 of the Supplemental Reply, emphasis in original):

> In sum, given applicants' explicit teaching that Tespec PRO-1 includes both the serine and histidine active site signatures and the fact that skilled workers recognized that, at the time the application was filed, ***"if a protein includes both the serine and histidine active site signatures, the probability of it being a trypsin family serine protease is 100%"***, then there can be little question that compositions falling within the scope of applicants' claims have a readily apparent utility as trypsin serine proteases or DNA molecules encoding such proteases.

In view of the fact that, "[i]n most cases, an applicant's assertion of utility creates a presumption of utility that will be sufficient to satisfy the utility requirement of 35 U.S.C. 101" (M.P.E.P. § 2107.02.III.A), the above-referenced assertions and evidence provided by applicants should have resulted in withdrawal of the utility rejection. The Office incorrectly maintained the utility rejection in the final Office action mailed on February 13, 2007, as well as in the Advisory action mailed on July 27, 2007, making the following two contentions (pages 3-4 of the final Office action):

> (A)...[T]he protein of SEQ ID NO: 2 does not have high homology to any protein

> with a demonstrated specific and substantial activity...Therefore, a specific and substantial utility for the polypeptide of SEQ ID NO: 2 cannot be deduced based on high homology to any protein with a well-established function...
>
> (B)...It is acknowledged that Applicants' arguments provide evidence that their Tespec PRO-2 polypeptide is a trypsin-family protease. However, evidence as a trypsin-family protease is not evidence of a specific and substantial, patentable utility...

Regarding point (A), as applicants note in the reply filed on July 13, 2007 (pages 5-6):

> A high degree of sequence homology is not the only way to determine that a protein belongs to a given class...The motifs contained in a protein sequence can be critical to a protein's function, and in some cases provide valuable information for identifying that function...high homology of the sequence of a protein to any serine protease is not required for the protein to be identified as a trypsin-family serine protease. Accordingly, given the teachings of the scientific literature, it would be unreasonable for the Office to doubt that the protein of SEQ ID NO: 2 having the serine and histidine active site signatures is a trypsin-family serine protease, irrespective of the degree of sequence homology to any other serine protease.

Indeed, in point (B), the Office acknowledges that applicants provided evidence that the Tespec PRO-2 polypeptide is a trypsin-family protease. Therefore, the only remaining question is whether identification as a trypsin-family serine protease is sufficient to establish specific and substantial patentable utility. Applicants address this point in the reply filed on July 13, 2007 (pages 4-5, emphasis in original):

> Example 10 [of the Training Materials] states: "...DNA ligases have a well-established use in the molecular biology art based on this class of protein's ability to ligase DNA." Under Example 10, once it is apparent that an identified protein belongs to a class of proteins having a particular function, and if diseases and/or substrates associated with the proteins that belong to the class are known in the art, such facts are sufficient to establish the specific and substantial utility of the identified protein. It is not necessary to provide additional evidence of specific diseases and/or substrates associated with the identified protein. Furthermore, applicants note that ligases are not all identical in either sequence or function – indeed, a variety of ligases with distinct substrate specificities are known – but the fact that the encoded protein of Example 10 belongs to the class of proteins with DNA ligase activity suffices to establish both specific and substantial utility. No more is required.
>
> Turning to the present case, trypsin-family serine proteases, like DNA ligases,

> have well-established, specific, and substantial uses in the molecular biology arts, and skilled artisans would readily recognize the utility of this class of proteins...Since specific activities and functions of trypsin-like serine proteases, as well as their utilities as targets for drugs, were known at the time of the present application, a skilled artisan would readily understand the utility of a protein that had been identified as a trypsin-like serine protease.

Thus, identification as a trypsin-family serine protease is sufficient to establish specific and substantial patentable utility.

In closing, applicants submit that the intent of the utility requirement, as provided in the Training Guidelines as well as 35 U.S.C. § 101, is not to require applicants to provide voluminous supporting evidence and analysis regarding asserted uses of a claimed invention. Rather, applicants' assertions of utility are generally to be accepted (M.P.E.P. § 2107.02.III.A), and only genuinely non-specific or non-substantial utilities are to be rejected. For example, the Training Guidelines note (page 5) that characterizations such as "gene probe" or "chromosome marker" are non-specific, as these are entirely generic descriptions that could apply to virtually any polynucleotide. Likewise, suggesting that a polypeptide may be used as an animal food supplement or shampoo ingredient would clearly be a non-substantial utility (Training Guidelines, page 7). In stark contrast to these examples, the presently-claimed invention has specific, substantial, credible, and well-established utility as a trypsin-family serine protease. The Office has provided no evidence to the contrary. Accordingly, the rejection for lack of utility should be withdrawn.

Applicants submit that the application is in condition for allowance, and this action is hereby respectfully requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: AUGUST 13, 2007

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